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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,166	03/31/2004	Robert Karlsson	B 522	7149

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GE HEALTHCARE BIO-SCIENCES CORP.
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/815,166	KARLSSON ET AL.	
	Examiner	Art Unit	
	GAIL R. GABEL	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7 and 10-19* is/are pending in the application.

4a) Of the above claim(s) *14-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/10/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 9/10/08 is acknowledged and has been entered. Claims 1-3 have been amended. Claims 5, 8, 9, and 20-34 have been cancelled. Claims 14-19 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Accordingly, claims 1-4, 6, 7, and 10-19 are pending. Claims 1-4, 6, 7, and 10-13 are under examination.

Withdrawn Rejections/Objections

2. All rejections or objections not reiterated herein, have been withdrawn.

3. The rejections of claims 5, 8, 9, and 20 are now moot in light of Applicant's cancellation of the claims.

4. In light of Applicant's amendment and arguments, the rejection of claims 1-4, 6, 7, and 10-13 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is hereby, withdrawn.

5. In light of Applicant's amendment and arguments, the rejection of claims 1-4, 6, 7, and 10-13 under 35 U.S.C. 103(a) as being unpatentable over Wahlstrom et al. (WO 96/38729) in view of Malmqvist et al. (US Patent 5,492,840), is hereby, withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-4, 6, 7, and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wahlstrom et al. (WO 96/38729) in view of Malmqvist et al. (US Patent 5,492,840) and in further view of Willmann et al. (US Patent 6,495,333).

Wahlstrom et al. teach a method of analyzing pathogenic cells (bacterial cells: Salmonella or Listeria) from a cell sample using modified inhibition type immunoassay method (p. 2, lines 11-29 and p. 3, lines 12-13). The method can also be used for application in detecting target cells expressing specific cell surface antigen or intracellular antigens present in blood sample (p. 3, lines 14-18). In practice, a predetermined amount of the cell sample is contacted with predetermined amount of

antibodies (i.e. ligands) that specifically bind antigens on the cells, and then allowed to bind. The bound cells are separated from the mixture to obtain a cell free solution which contains unbound ligands. Separation or removal of bound cells is performed by filtration or centrifugation method. The amount of unbound ligands or antibodies present in the solution is determined to provide detection of binding of ligands to the cells; thereby, indicating the presence of pathogenic or target cells present in the sample (p. 2, line 36 – p. 3, line 8 and p. 3, lines 24-26). Wahlstrom et al. specifically teach that the ligands are preferably added in predetermined excess amounts corresponding to the expected maximum amount of target cells, to leave unbound ligands in the reaction mixture (p. 3, lines 9-11). The amount of excess unbound ligand in the cell free solution is determined using a biosensor (solid phase) surface having immobilized thereto, binding partners or receptors that bind the unbound antibodies (p. 3, lines 29-36 and p. 4, lines 18-23). The measurement is advantageously based on evanescent wave sensing, such as surface Plasmon resonance spectroscopy, evanescent wave ellipsometry, optical waveguide sensors, etc. (p. 4, line 36 – p. 5, line 28). The biosensor surface may be provided in a flow cell (see p. 4, lines 1-3).

Wahlstrom et al. differ from the instant invention in failing to teach that the solid phase surface (biosensor) having immobilized thereto, different binding agents at defined positions on the surface, is initially contacted with a set of different ligands or antibodies that specifically bind antigens present on the target cells and which also bind the receptors or binding agents present on the surface, so as to determine the amount of binding of each of the ligands to the solid support surface.

Malmqvist et al. disclose biosensors and methods for functionalizing sensing surfaces to be used in systems for simultaneously measuring the concentrations of a plurality of different biomolecules in a sample (Abstract). When measurements are carried out, the sensing surfaces are first functionalized with different binding agents or ligands for selective interaction with different desired biomolecules (c. 2, line 66 – c. 3, line 28 and c. 4, lines 17-30). Malmqvist et al. specifically teach that ligands employed may be [hetero]bifunctional or polyfunctional ligand molecules which contain anti-f function which is utilized for immobilization into corresponding sensing surface and anti-f1-L1 to anti-fn-Ln function for bioselective function for interaction and coupling to different ligands and different biomolecules present in the sample solution (c. 4, lines 31-46 and c. 6, line 54 – c. 7, line 32). Malmqvist et al. also provide that the sensing surface may be regenerated at two different levels, either for binding a new analyte or for refunctionalizing the surface with the same or other heterobifunctional ligand molecules (c. 8, lines 23-26).

One of ordinary skill in the art at the time of the instant invention would have reasonable expectation of success in incorporating the teaching of Malmqvist in initially functionalizing the biosensor sensing surfaces with heterobifunctional ligands for binding and detection of the presence of analyte in a sample into the method of analyzing a cell sample for cell associated analytes as taught by Wahlstrom because Malmqvist specifically taught that his method allows for simultaneous measurement of several properties of one biomolecule or analyte, as well as simultaneous measurement of a plurality of analytes as those present in a cell sample.

Wahlstrom et al. and Malmqvist et al. do not teach permeabilizing cell membranes so as to render cells permeable to ligands.

Willmann teach permeabilizing cell membranes of nucleated cells using permeabilizing solution so as to allow ligands (antibodies) to permeate the cell membrane and bind to intracellular antigens. See Figure 1.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to permeabilize the cell membranes of cells in the method of Wahlstrom as modified by Malmqvist, using permeabilization solution as taught by Willmann for allowing ligands to permeate cell membrane and bind to intracellular antigens because Willmann specifically taught that cell membranes are impermeable to stains or antibody conjugated labels and that use of permeabilization solutions to render cell membranes permeable to stains is conventionally known in cell-based immunological assays, to permit contact and binding between labeled ligands and intracellular antigens specific thereto and to allow for detection and quantitation of intracellular proteins/analytes.

Response to Arguments

7. Applicant's arguments filed September 10, 2008 have been fully considered but they are not persuasive.

A) Applicant argues that there is an additional feature that distinguishes the presently claimed invention from the Wahlstrom et al. reference, because although it teaches a competitive assay, the method relies upon separation of antibody-antigen

components prior to analysis. Applicant then contends that this separation step is not required in the claimed invention because at high linear flow rates, cells and cell fragments do not readily migrate down to the sensor surface.

In response, the instant rejection based on the combination of Wahlstrom with Malmqvist and Willmann renders obvious the claimed invention because the claimed invention recites "comprising" language which does not exclude the separation step taught by Wahlstrom. Simply, in using the comprising language in claim 1, the separation step which is deemed not to be required in Applicant's invention is not excluded by the claims. Accordingly, the combined teaching of Wahlstrom with Malmqvist and Willmann reads on and suggests the claimed invention.

The transitional term "comprising" is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Mars Inc. v. H.J. Heinz Co., 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term comprising,' the terms containing' and mixture' are open-ended.").< Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition comprising' in a method claim indicates that the claim is open-ended and allows for additional steps."); Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80

USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts").

8. No claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAIL R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday to Thursday, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

December 29, 2008